Aggressive B-cell Lymphoma Diagnostic Algorithm

Morphology: diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma (HGBCL), or Burkitt lymphoma

- BLYMF / B-Cell Lymphoma, FISH, Tissue
  MYC break-apart FISH probe (BAP) and IGH/MYC dual fusion FISH (D-FISH) probe

Positive for MYC rearrangement but negative for IGH/MYC fusion
- Negative for MYC rearrangement and positive for IGH/MYC fusion
- Positive for MYC rearrangement and/or positive for IGH/MYC fusion

Negative for MYC rearrangement
- Burkitt lymphoma likely excluded, however:
  - Consider CMA/Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded for 11q23 aberrancy and 11q24-ter deletion
  - Consider D-FISH for IGK/MYC and IGL/MYC to exclude a MYC rearrangement completely, especially in a pediatric patient

FISH: BCL2 and BCL6/BAP
- Add IGK/MYC and IGL/MYC D-FISH only if pediatric patient and/or high suspicion for Burkitt lymphoma

Positive for MYC rearrangement but negative for IGH/MYC fusion
- Negative for MYC rearrangement and positive for IGH/MYC fusion

Morphology: DLBCL vs HGBCL
- Morphology: DLBCL vs Burkitt lymphoma

FISH: BCL2 and BCL6
- Burkitt lymphoma likely excluded, however:
  - Consider CMA/Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded for 11q23 aberrancy and 11q24-ter deletion
  - Consider D-FISH for IGK/MYC and IGL/MYC to exclude a MYC rearrangement completely, especially in a pediatric patient

Morphology: DLBCL vs HGBCL
- Morphology: DLBCL vs Burkitt lymphoma

Negative for BCL2 and BCL6 rearrangements
- Positive for BCL2 and/or BCL6 rearrangements

High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements
- Cell of origin (COO) immunohistochemistry (IHC) (CD10, BCL6, MUM1) and double expresser IHC (BCL2 and MYC)

Double expresser IHC: BCL2 and MYC
- All others

COO IHC: CD10
- POSITIVE
- NEGATIVE
  - BCL2+ and MYC+
  - Double expresser
  - Not a double expresser

CD10+, CD43+, BCL2+, MUM1+, MYC+, BCL2−
- Possibly Burkitt lymphoma, particularly if IG/MYC identified. Confirm with morphology and clinical.

Non-germinal center B-cell phenotype
- MUM1
- Non-germinal center B-cell phenotype

Germinal center B-cell phenotype
- Germinal center B-cell phenotype

HGBCL vs Burkitt lymphoma
- DLBCL

Cell of origin (COO) immunohistochemistry (IHC) (CD10, BCL6, MUM1) and double expresser IHC (BCL2 and MYC)
- High-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements

Any other phenotype
- CD10+, CD43+, BCL2+, MUM1+, MYC+, BCL2−

Germinal center B-cell phenotype
- HGBCL, not otherwise specified

Non-germinal center B-cell phenotype
- Probably Burkitt lymphoma, particularly if IG/MYC identified. Confirm with morphology and clinical.

HGBCL, not otherwise specified
- COO IHC (CD10, BCL6, MUM1) and double expresser IHC (BCL2 and MYC)